

## Abstract 274

**TITLE:** Topical Microbicide Research and Development at NIAID

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**ISSUE:** Sexual transmission of HIV continues to occur throughout the world despite the availability of latex condoms that, when used consistently and correctly, can prevent HIV infection. Reasons for lack of effective condom utilization the inability of the receptive partner to negotiate condom use; physical discomfort; trust issues, and decreased sexual pleasure. Topical microbicides (chemical formulations such as gels, creams, films, foams, tablets, and suppositories that are applied topically to genital mucosal surfaces) represent one approach to the prevention of sexual transmission of HIV and other STDs that may address these issues.

**PROGRAM:** To achieve the goal of developing a safe and effective topical microbicide, NIAID has established an integrated program of basic research, preclinical product development, clinical trials, and behavioral research. Investigator-initiated basic research focuses on the design of *in vitro* and *in vivo* models of the early steps in the infectious process of STD pathogens as well as on the biology and toxicology of genital mucosal surfaces. Preclinical product development encompasses the identification of promising active agents, establishment of safety and toxicity parameters in small animal models, development of topical formulations, and assessment of efficacy in animal models. Safety and efficacy of candidate microbicides are assessed in Phase I, II, and III clinical trials.

**RESULTS:** NIAID is presently supporting four topical microbicide program project grants focused on the development of clinically relevant *in vitro* and animal models for HIV, chlamydia, HPV, and HSV along with a portfolio of grants investigating mechanisms of mucosal HIV transmission and development of primate models. Accomplishments in preclinical microbicide development include establishment of a database of 1200 potential HIV blocking compounds; large-scale *in vitro* screening of candidate agents; rabbit vaginal irritation studies of 6 candidate products; formulations development for 2 candidate agents; primate model efficacy testing of 2 products; and progress in the establishment of an FIV efficacy model as well as a cell-associated model for vaginal SIV transmission. Two products have completed phase I safety trials with an additional two phase I trials scheduled to begin in spring 1999. In addition, phase II/III studies of N-9 products have been completed with a phase III study of an N9 gel scheduled to begin in fall, 1999.

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